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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,073	02/28/2005	Shigekazu Hokazono	HOKAZONO1	8315
1444 7590 07/09/2008 BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303				
EXAMINER RAMIREZ, DELIA M				
ART UNIT		PAPER NUMBER		
1652				
NOTIFICATION DATE		DELIVERY MODE		
07/09/2008		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mail@browdyneimark.com

Office Action Summary

Application No.

10/526,073

Applicant(s)

HOKAZONO ET AL.

Examiner

Delia M. Ramirez

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 February 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/5508)
- Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of the Application

Claims 1 and 6 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(c), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(c) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/12/2008 has been entered.

Amendment of claim 1, a new sequence listing, and a statement indicating that the new sequence listing does not introduce new matter into the disclosure, as submitted in a communication filed on 5/12/2008 are acknowledged.

Claims 1 and 6 are at issue and are being examined herein.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112, Second Paragraph

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
3. Claim 1 is indefinite in the recitation of "nucleic acid hybridizing to the nucleotide sequence of SEQ ID NO: 2 or a complementary strand thereof." for the following reasons. As previously indicated, hybridization only occurs among nucleic acid molecules and not with nucleotide sequences, which are graphical representations of how nucleotides are arranged in a molecule. In addition, the term "complementary" is unclear and confusing because fragments of any size which are complementary to the

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polynucleotides recited can be considered as “complementary”. Applicant has not define the term “complementary”, as it relates to size, in the specification either. If Applicant’s intended complementary nucleic acid is the entire full complement, it is suggested the term be amended to recite “full-length complementary”. For examination purposes, the suggested language will be used. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. Claim 1 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Amended claim 1 is directed to a genus of polypeptides encoded by a genus of nucleic acids which hybridize under specific conditions. However, there is no support for a washing temperature of 68 °C as now recited. The Examiner acknowledges that the specification refers to stringent conditions as “those described in Maniatis et al. (Molecular Cloning: A Laboratory Manual 2nd edition, Cold Spring Laboratories, 1989) or the like” (page 21, lines 21-25 of the specification). However there is no statement of incorporation by reference to the teachings of Maniatis et al. There is no indication in the specification that there was a clear intent to incorporate by reference the specific conditions disclosed in Maniatis et al. Furthermore, there is no disclosure in the specification that explicitly indicates 68 °C or the washing conditions as now recited as preferred embodiments of the genus of hybridization conditions. Applicant’s amendment is deemed an improper incorporation by reference. See 37 CFR 1.57. Accordingly, Applicant is requested to cancel the new matter in response to this Office action.

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6. Claim 1 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been discussed at length in previous Office actions. It is maintained for the reasons of record and those set forth below.

7. Applicant argues that the claim as amended now recites very stringent conditions. Specifically, applicant points out that the hybridization washing conditions now require a temperature of 68 °C. Thus, applicant request Applicant request withdrawal of the instant rejection.

8. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. While it is agreed that the hybridization conditions now recited would allow for 5.6% mismatching according to the McIninch and Wahl equation previously cited ($5.6\% = 73.6\text{ }^{\circ}\text{C} - 68\text{ }^{\circ}\text{C}$), there is no disclosure of a structure/function correlation which would allow one of skill in the art to recognize which of the many polynucleotides encompassed by the genus recited would encode a protein having thermostable ribonuclease H. The total number of variants of a polynucleotide having a specific sequence identity can be calculated from the formula $N! \times 3^A / (N-A)! \times A!$, where N is the length in nucleotides of the reference polynucleotide and A is the number of allowed substitutions for a specific % identity. Thus, for a variant of the polynucleotide of SEQ ID NO: 2 having 94.6% sequence identity to SEQ ID NO: 2, the total number of variants to be tested is $636! \times 3^{36} / (636-36)! \times 36!$ (SEQ ID NO: 2 has 636 nucleotides; 36 nucleotides = 0.056×636) or 1.24×10^{76} variants. There is no disclosure as to which 5.6% of the structure of the nucleic acid of SEQ ID NO: 2 can vary and still be able to encode a protein having thermostable ribonuclease H activity. There is no information as to which structural features in the essentially infinite number of variants encompassed by the claims are associated with the recited thermostable ribonuclease H activity. Thus, one cannot reasonably conclude that the teachings of the

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specification adequately describe the entire genus of polypeptides now recited. See, particularly, Example 11A of the revised Written Description Training Materials recently published for further guidance.

9. Claim 1 remains rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising SEQ ID NO: 1 or a polypeptide encoded by the nucleic acid of SEQ ID NO: 2, does not reasonably provide enablement for a polypeptide having thermostable ribonuclease H activity wherein said polypeptide is encoded by a nucleic acid which hybridizes under the recited conditions to the nucleic acid of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

10. This rejection has been discussed at length in previous Office actions and it is maintained for the reasons of record and those set forth below.

11. Applicant argues that the claim as amended now recites very stringent conditions. Specifically, applicant points out that the hybridization washing conditions now require a temperature of 68 C. Thus, applicant request Applicant request withdrawal of the instant rejection.

12. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. The level of mismatching associated with the conditions recited allows for proteins having 36 amino acid changes in the polypeptide of SEQ ID NO: 1 ($36 = 0.056 \times 636$; SEQ ID NO:2 = 636 nucleotides) as each nucleotide mismatch can potentially affect a codon. That potentially encompasses proteins having at least 83% sequence identity to the polypeptide of SEQ ID NO: 1 ($83\% = 100 - 36 \times 100 / 211$). Using the previously presented formula to calculate all the possible variants having a specific number of substitutions, the total number of variants of the polypeptide of SEQ ID NO: 1 having 36 substitutions amounts to 5.8×10^{87} variants. Thus, the number of variants to be tested without any

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guidance as to which variants are more likely to have the recited activity is essentially infinite. This amount of experimentation is undue as the specification has not provided any teaching or suggestion as to the structural features more likely to be associated with the recited function. Therefore, one cannot reasonably conclude that the claimed genus of polypeptides is fully enabled by the teachings of the specification and/or the prior art.

Claim Rejections - 35 USC § 102

13. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
14. Claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Klenk et al. (PIR accession number E69327, 1997). This rejection has been discussed at length in previous Office actions.
15. In view of Applicant's amendment of claim 1, which now requires a polypeptide encoded by a nucleic acid which hybridizes under conditions that would allow approximately 5.6% mismatching and the nucleic acid of Klenk et al. is less than 94.4% sequence identical to the polynucleotide of SEQ ID NO: 2, this rejection is hereby withdrawn.

Allowable Subject Matter

16. Claim 6 appear to be allowable over the prior art of record.

Conclusion

17. No claim is in condition for allowance.
18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through

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Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashaat Nashed can be reached on (571) 272-0934. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

/Delia M. Ramirez/

Delia M. Ramirez, Ph.D.
Primary Patent Examiner
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DR
July 8, 2008